Highly efficient synthesis and characterization of the GPR30-selective agonist G-1 and related tetrahydroquinoline analogs†

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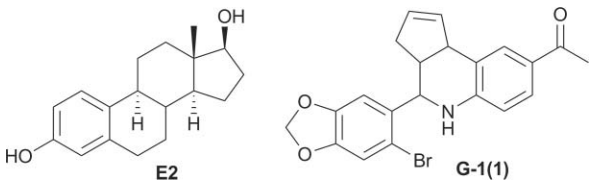
Received 20th January 2010, Accepted 25th February 2010
First published as an Advance Article on the web 16th March 2010
DOI: 10.1039/c001307b

The GPR30 agonist probe **G-1** and structural analogs were efficiently synthesized using multicomponent or stepwise Sc(III)-catalyzed aza-Diels–Alder cyclization. Optimization of solvent and reaction temperature provided enhanced *endo*-diastereoselectivity.

Introduction

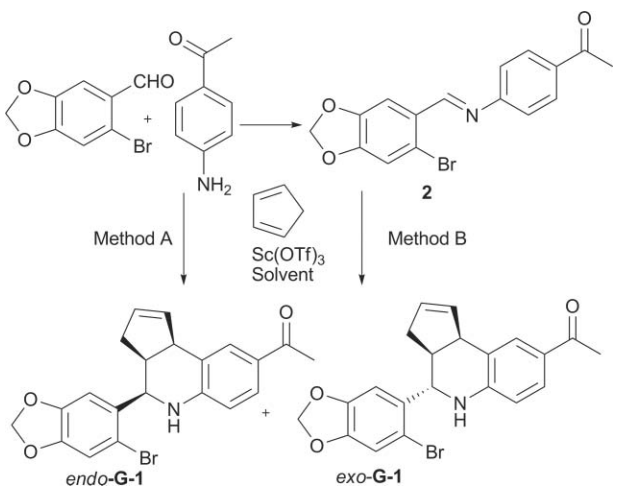
The discovery of the G protein-coupled estrogen receptor GPR30, (IUPHAR designation: GPER), has revealed a new pathway for non-genomic estrogen signaling. This 7-transmembrane G-protein coupled receptor is expressed in tissues throughout the body and implicated in several biologically important signaling pathways that affect normal and pathogenic states including cancer, reproduction, neuroendocrine and cardiovascular systems.[1] Distinguishing the different biological roles of GPR30 from the classical nuclear estrogen receptors (ERα/β) is complicated by similarities in ligand specificity for 17β -estradiol (**E2**) and xenoestrogens, with overlapping cellular responses mediated by distinct signaling pathways. The development of GPR30-selective chemical probes would provide valuable molecular tools to distinguish these complex systems *in vitro* and *in vivo*.



Recently, a combined virtual and biomolecular screen identified the first GPR30-selective agonist **G-1** (**1**), a substituted tetrahydro-3*H*-cyclopenta[*c*]quinoline.[2] This compound has been used to investigate GPR30-mediated biological effects in a wide variety of different cell types and *in vivo* models.[3] An evaluation of chemical probes developed through the National Institutes of Health Molecular Libraries and Imaging initiative rated **G-1** with high confidence for use *in vitro* and *in vivo*.[4] Therefore, we were interested in developing a high yield, diastereoselective preparative scale synthesis of **G-1** to provide sufficient quantities for expanded biological studies, and for construction of related analogs to investigate structure–activity relationships of GPR30-mediated signaling.

Results and discussion

The tetrahydroquinoline scaffold is accessible using the three-component aza-Diels–Alder (Povarov) reaction that can be catalyzed by a variety of Brønsted and Lewis acids.[5] We sought conditions that would provide rapid reaction times, maximum product yields, and increased diastereoselectivity favoring the *endo*- or *syn*-product in comparison with the original synthesis that achieved ~70% yield employing trifluoroacetic acid.[2] Following the precedent for lanthanide catalysis,[6] we found $Sc(OTf)_3$ effected the cyclization of 6-bromopiperonal, *p*-aminoacetophenone and cyclopentadiene in acetonitrile (MeCN) to produce **G-1** in near quantitative yield (Scheme 1, Table 1). This procedure was successfully performed on a multi-gram scale. The *endo* diastereomer was obtained as the major product; the *syn* orientation of protons



Scheme 1 Improved synthesis of **G-1**.

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† Electronic supplementary information (ESI) available: Crystallographic data for **G-1**; experimental procedures; copies of ^1H and ^{13}C NMR spectra; HPLC-MS, HRMS and other characterization data for new compounds. CCDC reference number 762397. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c001307b

Table 1 Optimization of **G-1** synthesis

Entry	Method[a,b]	Solvent	Time/h	*T*/°C	Yield (%)	*endo* : *exo*
1	A, B	MeCN	2	rt	98	94 : 6
2	A	MeCN	3	0	40	94 : 6
3	B	MeCN	3	0	98	97 : 3
4	A, B	DCM	2	rt	94	94 : 6
5	A	DCM	4	0	80	95 : 5
6	B	DCM	4	0	95	98 : 2

[a] A: Multicomponent cyclization. [b] B: Stepwise imine formation, cyclization.

H-3a and H-4 was assigned by the characteristic scalar coupling constant J (3a, 4) = 3.1 Hz, compared with significantly higher coupling constant for the *exo* diastereomer J (3a, 4) = 9.4 Hz. Recrystallization from acetonitrile did not further affect the diastereomer ratio.

Crystals of **G-1** suitable for X-ray diffraction were grown by slow evaporation from acetonitrile–methanol (1 : 1). The ORTEP structure of **G-1** confirms the structural assignment based on ^{1}H NMR exhibiting the *endo* orientation of cyclopentene ring with the 4-piperonal moiety (Fig. 1). Superimposing the X-ray and computed structures of **G-1** revealed only a slight difference in the conformation of the acetyl substituent. In the calculated conformation this group aligns with the plane defined by the tetrahydroquinoline ring system, but was rotated at a 15° angle in the crystal structure.

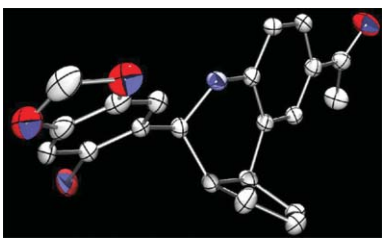


Fig. 1 X-Ray ORTEP Rendition of GPR-30 Agonist **G-1**.

In order to assess the reaction parameters with regards to product yields and optimize the *endo*-diastereoselectivity, we evaluated the cyclization in different solvents, and using a stepwise procedure employing the isolated imine (Schiff base). Imines are typically prepared using dehydrating agents or azeotropic removal of water, and recent examples include ionic liquids and microwave heating.[7] A simple procedure involving heating the neat aniline and aldehyde components at 170 °C for 5 min provided complete conversion to the desired imine, and subsequent Sc(III)-catalyzed cyclization with cyclopentadiene yielded the desired product (method B).

The yields and diastereoselectivities were identical for both methods at ambient temperature, but reducing the cyclization temperature to 0 °C and using dichloromethane (DCM) as the solvent achieved the highest *endo*-selectivity (entry 6, Table 1).

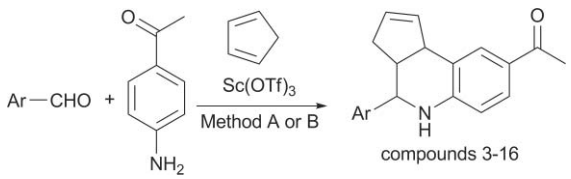
We prepared a series of tetrahydroquinoline analogs from a variety of substituted aldehydes using the multicomponent procedure (Table 2). These conditions were generally effective, but gave relatively low yields for the 4-methoxy- and 4-hydroxybenzaldehyde substrates (entries 3 and 5). The 3-substituted analogs gave higher relative yields (entries 4 and 6). We hypothesized that resonance inhibited formation of the Schiff base intermediates due to the strong electron-donating substituents at the 4-position. Consistent with these expectations, the stepwise procedure for Sc(III)-catalyzed imine cyclization increased product yields. Both methods gave similar results for the catechol analog that is a competitive ligand for the Lewis acid, and the intermediate imine exhibited low solubility under the reaction conditions (entry 7). Increased amounts of the *exo*-products were observed using 3-nitrobenzaldehyde, 3-formylthiophene and formylcyclohexene (entries 12–14), reflecting a trend for decreasing *endo*-diastereoselectivity associated with more electrophilic imine intermediates.

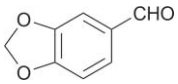
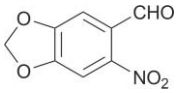
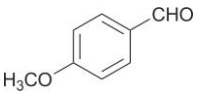
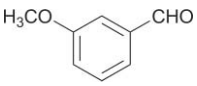
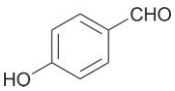
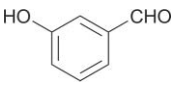
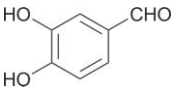
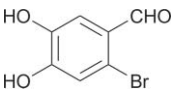
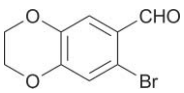
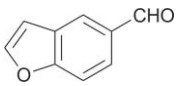
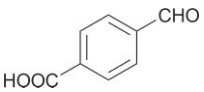
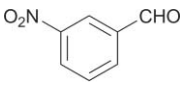
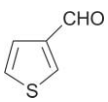
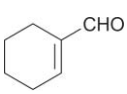
The analogous $Sc(OTf)_3$-mediated multi-component cyclization employing 2,3-dihydrofuran (2 eq) as the hetero-dienophile in MeCN at ambient temperature produced the isostructural furo[3,2-*c*]quinoline derivative **17** in moderate yield with low diastereoselectivity (Table 3).[8] The *syn* orientation of protons H-3a and H-4 in **17**-*endo* are evident from ^{1}H NMR scalar coupling constants of 3 Hz at 5.1 ppm, whereas protons in the *anti* orientation correspond to J (3a, 4) = 10.5 Hz at 4.5 ppm. The low *endo*/*exo* ratio is consistent with other examples of Povarov cyclizations employing 2,3-dihydrofuran as an aza-dienophile, and accentuates the different stereochemical outcome in comparison with cyclopentadiene.[6h,8a]

We required the isostructural *endo*-isomer of **17** for comparison of biological activity with **G-1** and attempted to optimize the diastereoselectivity of this reaction. Increasing the amount of 2,3-dihydrofuran from 2 to 10 equiv was detrimental to the yield of **17** (entry 2). Under these conditions 2,3-dihydrofuran undergoes ring opening to highly reactive 4-hydroxybutanal that results in formation of the undesired side product **18** from domino coupling.[9] The *exo*-diastereomer was slightly increased using the stepwise procedure (entry 3). Methanol has been successfully used as a solvent for sulfamic acid-catalyzed Povarov cyclizations employing 2,3-dihydrofuran. However, under these conditions the Sc(III)-catalyzed procedure gave low yields and increased amounts of *exo*-product, accompanied by the undesired byproduct **19** that incorporates methanol through a 4-component coupling process (entry 5).[8d,10] These results suggest the reaction with 2,3-dihydrofuran proceeds with a high degree of charge development under these conditions. The desired **17**-*endo* product was obtained as the major isomer (>70%) employing the stepwise reaction in dichloromethane, 1,4-dioxane and toluene at 0 °C. Further improvement in the *endo* : *exo* ratio were achieved using mixed solvents containing toluene or dioxane, and by increasing the concentration of the reaction mixture (entries 9–11). The preferential precipitation of the *exo* isomer enabled efficient separation of the diastereomers by recrystallization from acetonitrile–water.

Mechanistic studies suggest that Povarov cyclizations can proceed through concerted [4+2] aza-Diels Alder or stepwise pathways.[5l] The isolation of nucleophilic imine-addition product **19** indicates the stepwise process is favored for the electron rich alkene 2,3-dihydrofuran in polar alcohol solvent.[10] Solvent polarity affects charge development and synchronicity of bond formation in the transition state, and plays a significant role in determining the stereochemical outcome. Complexation of the Sc(III) catalyst induces polarization of the Schiff base intermediate, thereby altering the orbital energies and possibly enhancing the contributions of secondary interactions with the

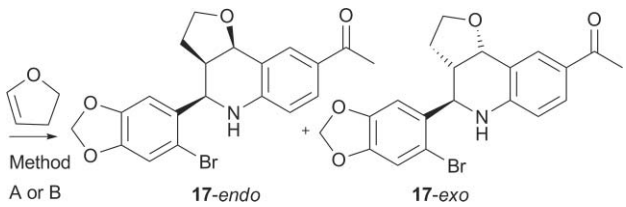
Table 2 Synthesis of tetrahydroquinoline analogs



Entry	Aldehyde	Method[a,b]	Time/h	Product	Yield (%)[c]	*endo* : *exo*[d]
1		A	2.0	**3**	88	93 : 7
2		A	3.0	**4**	95	95 : 5
3		A B	5.0 2.5	**5** **5**	75 90	91 : 9 92 : 8
4		A	2.0	**6**	95	92 : 8
5		A B	5.0 15.0	**7** **7**	70 80	95 : 5 96 : 4
6		A	1.5	**8**	95	96 : 4
7		A B	5.0 15.0	**9** **9**	70 72	92 : 8 92 : 8
8		A	2.0	**10**	77	93 : 7
9		A	3.0	**11**	84	92 : 8
10		A	3.0	**12**	92	92 : 8
11		A	2.5	**13**	92	92 : 8
12		A	1.0	**14**	98	89 : 11
13		A	1.5	**15**	94	80 : 20
14		A	1.0	**16**	90	63 : 37

[a] A: Multicomponent procedure. [b] B: Stepwise imine formation, cyclization. [c] Isolated yields. [d] *Endo* : *exo* ratio determined by ^{1}H NMR and HPLC.

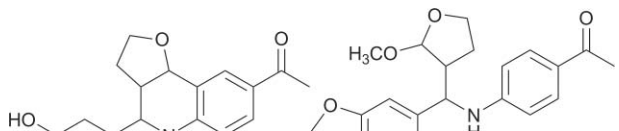
Table 3 Synthesis of furo[3,2-*c*]quinoline analogs



Entry	Method[a,b]	Solvent	Time/h	*T*/°C	Yield (%)	*endo* : *exo*[g]
1	A	MeCN[d]	5	rt	55	40 : 60
2	A	MeCN[e]	2	rt	15	50 : 50
3	B	MeCN[c]	2	rt	68	44 : 56
4	B	MeCN[c]	5	0	50	44 : 56
5	B	MeOH[c]	4	rt	6	27 : 73
6	B	DCM[c]	5	0	65	72 : 28
7	B	Dioxane[c]	3	0	52	75 : 25
8	B	Toluene[c]	5	0	45	77 : 23
9	B	DCM–Toluene[c]	5	0	54	82 : 18
10	B	DCM–Dioxane[c]	3	0	48	80 : 20
11	B	DCM[f]	3	0	50	84 : 16

[a] A: Multicomponent procedure. [b] B: Stepwise imine formation, cyclization. [c] 0.12 mmol of imine/mL of solvent and 2 eq. of 2,3-dihydrofuran. [d] 0.12 mmol of aldehyde and amine/mL and 3 eq. of 2,3-dihydrofuran. [e] 0.12 mmol of aldehyde and amine/mL and 10 eq. of 2,3-dihydrofuran. [f] 0.5 mmol of imine/mL and 2 eq. of 2,3-dihydrofuran. [g] *Endo* : *exo* ratio determined by ^{1}H NMR and HPLC.

alkene component in non-polar solvents. The solvent effects observed in this study correlate increased *endo*-selectivity for the Sc(III)-catalyzed reactions of 2,3-dihydrofuran with decreased dielectric constant of the solvent and reducing the cycloaddition temperature. These results are consistent with a kinetic model in which the *endo* orientation is favored by π–π contact dispersion interactions, and preference for the transition state with minimum charge development as the main factors governing the observed stereoselectivity.



Conclusions

We have developed an efficient, diastereoselective synthesis of the GPR30 agonist **G-1** and related analogs. The *endo*-structure of **G-1** originally assigned on the basis of ^{1}H NMR was verified by single crystal X-ray diffraction. A simple stepwise procedure involving formation of the imine by melting was employed in cases where the multicomponent approach was problematic, and provided increased product yields and *endo*-diastereoselectivity. The observed solvent effects provide guidance for ongoing efforts to develop related catalytic enantioselective cyclization procedures. The biological activities of these synthetic analogs 3–17 are currently under investigation.

Experimental

All reactions were performed in an efficient fume hood. Solvents and reagents were purchased from commercial sources and were used without further purification. Air sensitive reagents were stored in a glove box and handled according to accepted procedures. Chromatographic separations were performed using medium pressure flash chromatography and ethyl acetate/hexanes as eluent. Deuterated solvents were used without further purification. NMR spectra were acquired at ambient temperatures (18 ± 2 °C) unless otherwise noted. The ^{1}H NMR spectra in $CDCl_3$ were referenced to TMS unless otherwise noted. The ^{13}C {1H} NMR spectra were recorded at 75 or 100 MHz and referenced relative to the ^{13}C {1H} peaks of the solvent. Spectra are reported as (ppm), (multiplicity, coupling constants (Hz), and number of protons). HPLC–MS was performed using a C18 (5 μm, 3.0 × 150 mm) column.

Method A representative multicomponent procedure

(1-[4-(6-Bromobenzo[1,3]dioxol-5-yl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl]-ethanone) (G-1). A catalytic amount of $Sc(OTf)_3$ (0.492 g, 1.0 mmol) in anhydrous acetonitrile (2.0 cm^3) was added to the mixture of 6-bromopiperonal (2.30 g, 10.0 mmol), *p*-aminoacetophenone (1.30 g, 10.0 mmol) and cyclopentadiene (3.30 g, 50.0 mmol) in acetonitrile (25 cm^3). The reaction mixture was stirred at ambient temperature (~23 °C) for 2.0 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to provide **G-1** (4.03 g, 98%, *endo* : *exo* = 94 : 6) as a white solid. mp: 103–105 °C; FT-IR (KBr, cm^{-1}) 3324, 2895, 1659, 1596, 1474; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.70 (1 H, d, *J* 1.6, Ar), 7.61 (1 H, dd, *J* 8.3, 1.6, Ar) 7.09 (1 H, s, Ar), 7.03 (1 H, s, Ar), 6.61 (1 H, d, *J* 8.3, Ar), 6.00 (1 H, d, *J* 1.3, OCH_2O), 5.99 (1 H, d, *J* 1.3, OCH_2O), 5.96-5.92 (1 H, m, CH=*CH*), 5.68-5.66 (1 H, m, CH=*CH*), 4.98 (1 H, d, *J* 3.1, Ar*CH*NH), 4.12 (1 H, d, *J* 8.3, Ar*CH*CH=CH), 4.02 (1 H, br s, NH), 3.23-3.15 (1 H, m, CH_2CH=CH(1H)), 2.57-2.46 (4 H, m, CH_2CH=CH(1H) and COCH_3), 1.86-1.77 (1 H, m, CH_2CHCH); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 149.9, 147.6, 147.5, 133.8, 133.6, 130.4, 130.0, 128.7, 127.6, 125.1, 115.2, 113.1, 112.9, 107.7, 101.8, 56.2, 45.4, 42.0, 31.4, 26.1; HPLC-MS: Elution with 60–90% CH_3CN in H_2O (gradient 1.5% min^{-1}), exhibited a peak at 12.42 min. ESI-MS *m*/*z* (ES+) calcd for $C_{21}H_{18}BrNO_3$ $(M+H)^+$ 412.05; found 412.18.

Method B general procedure for stepwise cyclization

The aniline (1 mmol) and aldehyde (1 mmol) were dissolved in methanol (2 cm^3) then concentrated *in vacuo*. The resulting viscous oil was heated at 170–180 °C under an argon atmosphere for 5 min. The volatiles were removed to provide the corresponding imine. The imine was dissolved in the specified solvent (4 cm^3), then cyclopentadiene (0.330 g, 5.0 mmol) and a solution of scandium triflate (0.049 g, 0.1 mmol) in the solvent (0.5 mL) were added, and the reaction was stirred at the specified temperature for 2–15 h. The product formation was monitored by thin layer chromatography using ethyl acetate/hexanes eluent. The volatiles were removed *in vacuo*. The crude product was purified as specified. The *endo*:*exo* ratio of the product was determined by integration of the ^{1}H NMR spectra and HPLC chromatograms.

***E*-1-(4-((6-Bromobenzo[*d*][1,3]dioxol-5-yl)methyleneamino)-phenyl)ethanone (2).** Following Method B *p*-aminoacetophenone (0.135 g, 1 mmol) and 6-bromopiperonal (0.229 g, 1 mmol) were combined to provide the imine **2** (0.346 g, 100%) as a pale yellow solid. mp: 155–158 °C; ν_{max}(KBr)/cm^{-1} 1675, 1580, 1483, 1261, 1041; δ_H (300 MHz; $CDCl_3$; Me_4Si) 8.70 (1 H, s), 8.00 (2 H, d, *J* 7.8), 7.70 (1 H, s), 7.22 (2 H, d, *J* 7.8), 7.05 (1 H, s) 6.06 (2 H, s), 2.61 (3 H, s); δ_C (75 MHz; $CDCl_3$; Me_4Si) 197.1, 159.9, 155.9, 151.4, 147.9, 134.6, 129.7, 128.1, 121.0, 119.3, 112.8, 107.8, 102.3, 26.5.

1-((3a*S*,4*R*,9b*R*)-4-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl)ethanone (G-1). Following Method B a catalytic amount of $Sc(OTf)_3$ (0.049 g, 0.1 mmol) in DCM (0.2 cm^3) was added to the mixture of imine, **2** (0.346 g, 1 mmol) and cyclopentadiene (0.330 g, 5.0 mmol) in DCM (4 cm^3). The reaction mixture was stirred at 0 °C for 4.0 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to provide **G-1** (0.390 g, 95%, *endo* : *exo* = 98 : 02) as a white solid.

1-(4-Benzo[1,3]dioxol-5-yl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl)-ethanone (3). Following Method A piperonal (0.075 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol) and cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were combined in anhydrous acetonitrile (2 cm^3) and stirred for 2 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **3** (0.146 g, 88%, *endo* : *exo* = 93 : 7) as a colorless solid. mp: 66-68 °C; ν_{max}(KBr)/cm^{-1} 3324, 2887, 1651, 1596, 1228; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.69 (1 H, d, *J* 2.0), 7.59 (1 H, dd, *J* 8.5 and 2.0), 6.89-6.78 (3 H, m), 6.58 (1 H, d, *J* 8.5), 5.95 (2 H, s), 5.94-5.90 (1 H, m), 5.67-5.63 (1 H, m), 4.60 (1 H, d, *J* 3.2), 4.24 (1 H, br s), 4.08 (1 H, d, *J* 9.0), 2.97-2.91 (1 H, m), 2.54-2.52 (4 H, m), 1.90-1.81 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.4, 150.0, 147.7, 146.7, 135.7, 133.7, 130.4, 129.9, 128.3, 127.7, 124.8, 119.3, 114.8, 108.2, 106.7, 101.0, 57.0, 45.9, 45.5, 31.3, 25.9; HRMS (EI-MS): calcd [M+H]$^+$ for $C_{21}H_{19}NO_3$ 334.1443, found 334.1438.

1-[4-(6-Nitrobenzo[1,3]dioxol-5-yl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl]-ethanone (4). Following Method A 6-nitropiperonal (0.098 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were combined in anhydrous acetonitrile (2 cm^3) and stirred for 3 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **4** (0.180 g, 95%, *endo* : *exo* = 95 : 5) as a colorless solid. mp: 118-120 °C; ν_{max}(KBr)/cm^{-1} 3318, 2906, 1659, 1597, 1248; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.68 (1 H, d, *J* 2.0), 7.60 (1 H, dd, *J* 8.4 and 2.0), 7.48 (1 H, s), 7.34 (1 H, s), 6.61 (1 H, d, *J* 8.4), 6.14 (1 H, d, *J* 1.1), 6.13 (1 H, d, *J* 1.1), 5.99-5.95 (1 H, m), 5.75-5.65 (1 H, m), 5.26 (1 H, d, *J* 2.9), 4.14 (1 H, d, *J* 8.6), 4.07 (1 H, br s), 3.34-3.25 (1 H, m), 2.64-2.52 (1 H, m), 2.49 (3 H, s), 1.91-1.82 (1 H, m); δ_C (75 MHz; $CDCl_3$; Me_4Si) 196.5, 152.0, 149.5, 147.01, 142.6, 134.0, 133.8, 130.2, 130.1, 128.9, 127.5, 125.0, 115.3, 107.1, 105.7, 103.0, 52.7, 45.5, 43.2, 31.3, 20.0. HRMS (EI-MS): calcd [M+H]$^+$ for $C_{21}H_{18}N_2O_5$ 379.1294, found 379.1298.

1-[4-(4-Methoxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl]-ethanone (5). Following Method B the imine prepared from *p*-aminoacetophenone (0.067 g, 0.5 mmol) and 4-methoxybenzaldehyde (0.127 g, 0.5 mmol) was dissolved in dichloromethane (2 cm^3) at ambient temperature, then cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were added, and the mixture stirred for 2.5 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **5** (0.144 g, 90%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 58–60 °C; ν_{max}(KBr)/cm^{-1} 3338, 2928, 1658, 1596, 1284; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.69 (1 H, s), 7.61 (1 H, dd, *J* 8.4 and 2.0), 7.31 (2 H, d, *J* 8.8), 6.91 (2 H, d, *J* 8.8), 6.93 (1 H, d, *J* 8.4), 5.93-5.90 (1 H, m), 5.67-5.64 (1 H, m), 4.66 (1 H, d, *J* 3.1), 4.23 (1 H, s), 4.10 (1 H, d, *J* 8.4), 3.81 (3 H, s), 3.00-2.95 (1 H, m), 2.59-2.47 (4 H, m), 1.86-1.80 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.4, 159.0, 150.3, 133.9, 133.8, 13.5, 130.08, 128.4, 127.7, 127.6, 125.0, 114.8, 114.0, 56.9, 55.3, 46.0, 45.7, 31.5, 26.0; HRMS (EI-MS): calcd [M+H]$^+$ for $C_{21}H_{21}NO_2$ 320.1651, found 320.1660.

1-[4-(3-Methoxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl]-ethanone (6). Following Method A *m*-methoxybenzaldehyde (0.073 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3) and the mixture stirred for 2 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **6** (0.165 g, 95%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 56–58 °C; IR (KBr, cm^{-1}) 3337, 2931, 1656, 1596, 1285; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.71 (1 H, d, *J* 2.0), 7.62 (1 H, dd, *J* 8.4 and 2.0), 7.31 (1 H, m), 7.02-6.96 (2 H, m), 6.85 (1 H, dd, *J* 8.4 and 2.0), 6.60 (1 H, d, *J* 8.4), 5.93-5.89 (1 H, m), 5.68-5.65 (1 H, m), 4.69 (1 H, d, *J* 3.3), 4.23 (1 H, br s), 4.12 (1 H, d, *J* 8.6), 3.83 (3 H, s), 3.06-2.98 (1 H, m), 2.60-2.54 (1 H, m), 2.50 (3 H, s), 1.88-1.81 (1 H, m). δ_C(100 MHz; $CDCl_3$)196.6, 159.6, 150.1, 143.4, 133.6, 130.4, 129.9 129.4, 128.1, 127.6, 124.8, 118.5, 114.8, 112.4, 112.0, 57.1, 55.1, 45.6, 45.4, 31.4, 25.8; HRMS (EI-MS): calcd [M+H]$^+$ for $C_{21}H_{21}NO_2$ 320.1651, found 320.1655.

1-[4-(4-Hydroxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl]-ethanone (7). Following Method B, the imine prepared from *p*-aminoacetophenone (0.067 g, 0.5 mmol), 4-hydroxybenzaldehyde (0.061 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) was dissolved in dichloromethane (2 cm^3) at ambient temperature and the mixture stirred for 15 h. The volatiles were removed *in vacuo*. The residue was purified by recrystallization from chloroform (5 cm^3) to give the product **7** (0.125 g, 80%, *endo* : *exo* = 96 : 4) as a colorless solid. mp: 208–210 °C; ν_{max}(KBr)/cm^{-1} 3360, 2917, 1650, 1593, 1287; δ_H (300 MHz; CD_3COCD_3) 8.31 (1 H, d, *J* 2.0), 7.69 (1 H, m), 7.58 (1 H, d, *J* 8.4), 7.26 (2 H, d, *J* 8.4), 6.83 (2 H, d, *J* 8.4), 6.8 (1 H, s), 5.97-5.94 (1 H, m), 5.61-5.60 (1 H, m), 5.54 (1 H, s), 4.63 (1 H, d, *J* 3.3), 4.09 (1 H, d, *J* 8.6), 2.99-2.94 (1 H, m), 2.53-2.47 (1 H, m), 2.42 (3 H, s), 1.77-1.73 (1 H, m); δ_C (100 MHz; CD_3COCD_3) 195.7, 157.4, 152.0, 135.3, 133.9, 130.8, 130.6, 128.7, 128.4, 128.0, 125.3, 115.9, 115.7, 57.3, 47.1, 46.5, 32.2, 26.0. HRMS (EI-MS): calcd [M+H]$^+$ for $C_{20}H_{19}NO_2$ 306.1494, found 306.1506.

1-[4-(3-Hydroxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl]-ethanone (8). Following Method A *m*-hydroxybenzaldehyde (0.061 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.0246 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3), and the mixture stirred for 1.5 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **8** (0.150 g, 98%, *endo* : *exo* 96 : 4) as a colorless solid. mp: 210–212 °C; ν_{max}(KBr)/cm^{-1} 3346, 2936, 1640, 1599, 1296; δ_H(400 MHz, d_6-DMSO) 9.38 (1 H, s), 7.59 (1 H, d, *J* 2.0), 7.51 (1 H, dd, *J* 8.4 and 2.0), 7.15 (1 H, m), 6.84-6.83 (2 H, m), 6.75 (1 H, d, *J* 8.4), 6.66 (1 H, dd, *J* 8.4 and 1.6), 6.51 (1 H, s) 5.97-5.92 (1 H, m), 5.61-5.56 (1 H, m), 4.55 (1 H, d, *J* 2.6), 4.04 (1 H, d, *J* 8.6), 2.93-2.88 (1 H, m), 2.42-2.30 (4 H, m), 1.70-1.61 (1 H, m); δ_C (100 MHz; d_6-DMSO) 195.4, 157.2, 151.1, 143.5, 134.7 129.8, 129.6, 129.1, 127.0, 126.6, 123.6, 117.2, 114.7, 113.9, 113.3, 55.8, 45.2, 44.9, 31.4, 25.9; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{19}NO_2$ 306.1494, found 306.1495.

1-(4-(3,4-Dihydroxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl)ethanone (9). Following Method A 3,4-dihydroxybenzaldehyde (0.069 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3), and the mixture stirred for 5 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **9** (0.112 g, 70%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 95-97 °C; ν_{max}(KBr)/cm^{-1} 3485, 2932, 1658, 1589, 1282; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.68 (1 H, s), 7.60 (1 H, dd, *J* 8.5 and 2.0), 6.90-6.87 (2 H, m), 6.76 (1 H, dd, *J* 8.4 and 2.0), 6.49 (1 H, d, *J* 8.5), 5.85-5.83 (1 H, m), 5.60-5.57 (1 H, m), 4.50 (1 H, d, *J* 3.2), 4.22 (1 H, br s), 4.01 (1 H, d, *J* 8.9), 2.90-2.80 (1 H, m), 2.51-2.31 (4 H, m), 1.84-1.76 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 198.4, 150.9, 144.0, 143.4, 134.1, 133.6, 130.7, 130.5, 128.1, 127.5, 125.0, 118.4, 115.2, 114.9, 113.2, 56.7, 45.8, 45.5, 31.4, 26.0; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{19}NO_3$ 322.1443, found 322.1448.

1-[4-(2-Bromo-4,5-dihydroxyphenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl]-ethanone (10). Following Method A 2-bromo-4,5-dihydroxybenzaldehyde (0.217 g, 1 mmol), *p*-aminoacetophenone (0.135 g, 1 mmol), cyclopentadiene (0.330 g, 5 mmol) and $Sc(OTf)_3$ (0.049 g, 0.1 mmol) were dissolved in acetonitrile (4 cm^3), and the mixture stirred for 2 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **10** (0.308 g, 77%, *endo* : *exo* = 93 : 7) as a colorless solid. mp: 209–211 °C; ν_{max}(KBr)/cm^{-1} 3470, 2934, 1660, 1596, 1280; δ_H(300 MHz, d_6-DMSO) 9.29 (1 H br s) 7.60 (1 H, s), 7.52 (1 H, dd, *J* 8.5 and 2.0), 7.00 (1 H, s) 6.94 (1 H, s), 6.74 (1 H, d, *J* 8.5), 6.44 (1 H, br s), 5.98-5.93 (1 H, m), 5.65-5.60 (1 H, m), 4.69 (1 H, d, *J* 3.3), 4.02 (1 H d, *J* 8.5), 3.03-2.93 (1 H, m), 2.46-2.32 (4 H, m), 1.69-1.61 (1 H, m); δ_C(75 MHz, d_6-DMSO) 195.4, 151.1, 145.4, 145.0, 134.6, 130.3, 129.8, 129.6, 127.0, 126.8, 123.6, 118.9, 115.4, 114.8, 109.5, 54.7, 44.7, 42.0, 31.3, 26.0; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{18}BrNO_3$ 400.0548, found 400.0555.

1-[4-(7-Bromo-2,3-dihydrobenzo[1,4]dioxin-6-yl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-8-yl]-ethanone (11). Following Method A 7-bromo-2,3-dihydrobenzo[1,4]dioxine-6-carbaldehyde (0.121 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3) and the mixture stirred for 3 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **11** (0.180 g, 84%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 96–99 °C; ν_{max}(KBr)/cm^{-1} 3325, 28.95, 1659, 1598, 1228; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.69 (1 H, d, *J* 1.9), 7.61 (1 H, dd, *J* 8.3 and 1.9), 7.10 (1 H, s), 7.08 (1 H, s), 6.60 (1 H, d, *J* 8.3), 5.94-5.90 (1 H, m), 5.67-5.63 (1 H, m), 4.91 (1 H, d, *J* 3.2), 4.26 (4 H, s), 4.12 (1 H, d, *J* 8.8), 4.03 (1 H br s), 3.28-3.18 (1 H, m), 2.56-2.46 (4 H, m), 1.85-1.76 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 150.1, 143.3, 143.1, 133.8, 133.2, 130.4, 130.0, 128.6, 127.6, 125.2, 121.2, 116.2, 115.1, 112.8, 64.31, 55.77, 45.4, 42.0, 31.4, 26.0; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{22}H_{20}BrNO_3$ 426.0705, found 426.0690.

1-(4-Benzofuran-5-yl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[*c*]quinolin-8-yl)ethanone (12). Following Method A 1-benzofuran-5-carbaldehyde (0.165 g, 1.13 mmol), *p*-aminoacetophenone (0.152 g, 1.13 mmol), cyclopentadiene (0.330 g, 5.0 mmol) and $Sc(OTf)_3$ (0.055 g, 0.113 mmol) were dissolved in acetonitrile (4.5 cm^3), and the mixture stirred for 3 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **12** (0.342 g, 92%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 68–70 °C; ν_{max}(KBr)/cm^{-1} 3335, 2927, 1659, 1596, 1286; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.71 (1 H, d, *J* 2.0), 7.67-7.63 (2 H, m), 7.61 (1 H, dd, *J* 8.4 and 2.0), 7.49 (1 H, d, *J* 8.4), 7.32 (1 H, dd, *J* 8.6 and 1.7), 6.77-6.76 (1 H, m), 6.61 (1 H, d, *J* 8.4), 5.94- 5.90 (1 H, m), 5.67-5.64 (1 H, m), 4.80 (1 H, d, *J* 3.1), 4.33 (1 H, br s), 4.13 (1 H, d, *J* 8.4), 3.1-2.96 (1 H, m), 2.65-2.56 (1 H, m), 2.49 (3 H, s), 1.85-1.75 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 154.2, 150.2, 145.5, 136.4, 133.7, 130.5, 130.0, 128.3, 127.7, 127.6, 124.9, 122.8, 118.6, 144.8, 111.3, 106.5, 57.0, 46.1, 45.6, 31.4, 26.0; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{22}H_{19}NO_2$ 330.1494, found 330.1503.

4-(8-Acetyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-4-yl)-benzoic acid (13). Following Method A 4-formylbenzoic acid (0.075 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3), and the mixture stirred for 2.5 h. The product precipitated from the reaction mixture and was isolated by filtration and washed with acetonitrile to provide the product **13** (0.157 g, 95%, *endo* : *exo* = 92 : 8) as a colorless solid. mp: 252–255 °C; ν_{max}(KBr)/cm^{-1} 3365, 2951, 1642, 1710, 1288; δ_H (300 MHz, CD_3OD) 8.04 (2 H, d, *J* 8.2), 7.69 (1 H, d, *J* 2.1), 7.62 (1 H, dd, *J* 8.6 and 2.1), 7.57 (2 H, d, *J* 8.2), 6.74 (1 H, d, *J* 8.6), 5.95-5.93 (1 H, m), 5.62-5.60 (1 H, m), 4.78 (1 H, d, *J* 3.3), 4.18 (1 H, d, *J* 8.8), 3.07-2.98 (1 H, m), 2.51-2.44 (4 H, m), 1.72-1.67 (1 H, m). δ_C(75 MHz, d_6-DMSO) 195.5, 167.2, 150.8, 147.18, 134.7, 131.6, 129.8, 129.5, 129.3, 127.1, 126.9, 126.7, 123.6, 114.9, 55.7, 44.9, 44.8, 31.2, 26.0. HRMS (EI-MS): calcd $[M - H]^-$ for $C_{21}H_{19}NO_3$ 332.1292, found 332.1287.

1-(4-(3-Nitrophenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]-quinolin-8-yl)-ethanone (14). Following Method A *m*-nitrobenzaldehyde (0.075 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3), and the mixture stirred for 1 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate/hexanes (15 : 85) to isolate the product **14** (0.164 g, 98%, *endo*5 : *exo* = 89 : 11) as a yellow solid. mp: 175–176 °C; ν_{max}(KBr)/cm^{-1} 3310, 2914, 1658, 1576, 1367; δ_H(300 MHz; $CDCl_3$; Me_4Si) 8.31 (1 H, d, *J* 1.8), 8.18 (1 H, ddd, *J* 8.2, 2.4 and 1.0), 7.78-7.72 (2 H, m), 7.66-7.55 (2 H, m), 6.67 (1 H, d, *J* 8.5), 5.96-5.92 (1 H, m), 5.67-5.65 (1 H, m), 4.85 (1 H, d, *J* 3.5), 4.26 (1 H, br s), 4.16 (1 H, d, *J* 8.4), 3.10-3.03 (1 H, m), 2.60-2.51 (4 H, m), 1.82-1.73 (1 H, m). δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 149.3, 148.5, 144.2, 133.7, 132.5, 130.1, 129.9, 129.6, 129.0, 127.8, 124.8, 122.6, 121.2, 115.3, 56.8, 45.48, 45.45, 31.3, 26.1. HPLC-MS: Elution with 60-90% CH_3CN (gradient 1.5% min^{-1}) in H_2O, exhibited a single peak at 7.05 min. ESI-MS *m*/*z* [ES^+] calcd for $C_{20}H_{18}N_2O_3$ $[M+H]^+$ 335.13; found 335.13.

1-(4-Thiophen-3-yl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]-quinolin-8-yl)-ethanone (15). Following Method A thiophene-3-carbaldehyde (0.056 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.0246 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3) and the mixture stirred for 1.5 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **15** (0.138 g, 94%, *endo* : *exo* = 80 : 20) as colorless solid. mp: 144–147 °C. ν_{max}(KBr)/cm^{-1} 3338, 2912, 1647, 1597, 1292; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.68 (1 H, d, *J* 2.0), 7.59 (1 H, dd, *J* 8.5 and 2.0), 7.32 (1 H, m), 7.23-7.22 (1 H, m), 7.09 (1 H, dd, *J* 5.0 and 2.5), 6.39 (1 H, d, *J* 8.5), 5.90-5.85 (1 H, m), 5.67-5.64 (1 H, m), 4.78 (1 H, d, *J* 3.5), 4.34 (1 H, s), 4.10 (1 H, d, *J* 9.0), 3.08-2.98 (1 H, m), 2.61-2.50 (1 H, m), 2.47 (3H, s), 1.97-1.87 (1 H, m); δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 149.9, 143.1, 133.8, 130.4, 129.9, 128.4, 127.7, 126.1, 126.0, 125.1, 120.3, 114.8, 53.9, 45.4, 44.9, 31.9, 26.0; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{18}H_{17}NOS$ 296.1109, found 296.1115.

1-(4-Cyclohex-1-enyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]-quinolin-8-yl)-ethanone (16). Following Method A cyclohex-1-enecarbaldehyde (0.055 g, 0.5 mmol), *p*-aminoacetophenone (0.067 g, 0.5 mmol), cyclopentadiene (0.165 g, 2.5 mmol) and $Sc(OTf)_3$ (0.024 g, 0.05 mmol) were dissolved in acetonitrile (2 cm^3) and the mixture stirred for 1 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **16** (0.132 g, 90%, *endo* : *exo* = 63 : 37) as a colorless solid. mp: 173–175 °C; ν_{max}(KBr)/cm^{-1} 3377, 2934, 1647, 1599, 1274; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.64 (1 H, d, *J* 2.0), 7.57 (1 H, dd, *J* 8.5 and 2.0), 6.53 (1 H, dd, *J* 8.5 and 2.0), 5.89-5.87 (1 H, m), 5.73-5.70 (3 H, m), 4.28 (1 H, br s), 3.95 (1 H, d, *J* 8.8), 3.23-3.14 (1 H, m), 3.02-2.88 (1 H m), 2.50-2.42 (4 H, m), 2.22-1.81 (6 H, m), 1.68-1.63 (1 H, m), 1.38-1.28 (1 H, m). δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.3, 150.0, 149.9, 134.1, 130.2, 129.8, 127.7, 127.6, 127.2, 126.7, 125.5, 125.1, 125.0, 124.9, 114.34, 114.30, 57.4, 57.0, 45.6, 40.7, 40.5, 36.0, 35.9, 30.8, 30.7, 28.8, 27.8, 25.9, 25.6, 24.8, 24.5; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{23}NO$ 294.1858, found 294.1858.

1-[4-(6-Bromobenzo[1,3]dioxol-5-yl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-*c*]quinolin-8-yl]-ethanone (17-*exo*). Following Method B the imine prepared from *p*-aminoacetophenone (0.067 g, 0.5 mmol) and 6-bromopiperonal (0.173 g, 0.5 mmol) was dissolved in acetonitrile (4 cm^3) at ambient temperature, then 2,3-dihydrofuran (0.070 g, 1.0 mmol) and $Sc(OTf)_3$ (0.0246 g, 0.05 mmol) were added. The mixture was stirred for 2 h. The volatiles were removed *in vacuo*. The residue was purified by preparative silica gel column chromatography using ethyl acetate–hexanes (10 : 90) to isolate the product **17** (0.142 g, 68%, *endo* : *exo* = 44 : 56) as a colorless solid. The diastereomerically pure compounds were obtained by recrystallization from acetonitrile–water (2 : 1) which resulted in selective precipitation of **17-*exo*:** mp: 77–80 °C; ν_{max}(KBr)/cm^{-1} 3321, 2879, 1659, 1608, 1256; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.99 (1 H, d, *J* 2.0), 7.78 (1 H, dd, *J* 8.5 and 2.0), 7.03 (1 H, s), 6.99 (1 H, s), 6.62 (1 H, d, *J* 8.5), 6.01-6.00 (2 H, m), 4.62 (1 H, d, *J* 4.7), 4.54 (1 H, s), 4.51 (1 H, d, *J* 10.5), 4.14-4.06 (1 H, m), 3.97-3.89 (1 H, m), 2.52 (3 H, s), 2.43-2.36 (1 H, m), 2.13-2.06 (1 H, m), 1.87-1.80 (1 H, m). δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.3, 149.1, 148.1, 148.0, 133.01, 132.9, 129.6, 127.8, 118.3, 115.1, 114.2, 112.5, 108.4, 102.0, 75.6, 65.5, 54.4, 43.0, 28.2, 26.1; HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{18}BrNO_4$ 416.0497, found 416.0490.

1-[4-(6-Bromobenzo[1,3]dioxol-5-yl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-*c*]quinolin-8-yl]-ethanone (17-*endo*). **17-*endo***: mp: 99–101 °C; ν_{max}(KBr)/cm^{-1} 3325, 2881, 1660, 1609, 1254; δ_H(300 MHz; $CDCl_3$; Me_4Si) 7.97 (1 H, d, *J* 2.0), 7.75 (1 H, dd, *J* 8.5 and 2.0), 7.17 (1 H, s), 7.04 (1 H, s), 6.61 (1 H, d, *J* 8.5), 6.02 (1 H, d, *J* 1.3), 6.0 (1 H, d, *J* 1.3), 5.27 (1 H, d, *J* 7.8), 5.10 (1 H, d, *J* 3.0), 4.14 (1 H, br s), 3.85-3.76 (2 H, m), 3.00-2.92 (1 H, m), 2.53 (3 H, s), 2.10-2.02 (1 H, m), 1.56-1.50 (1H, m). δ_C(75 MHz; $CDCl_3$; Me_4Si) 196.5, 148.5, 147.8, 147.7, 132.8, 131.7, 128.8, 128.0 121.5, 114.7, 113.0, 112.9, 107.6, 101.9, 74.9, 66.8, 55.4, 41.5, 26.1, 24.6. HRMS (EI-MS): calcd $[M+H]^+$ for $C_{20}H_{18}BrNO_3$ 416.0497, found 416.0478.

Acknowledgements

This work was supported by NIH grants R01 CA127731, U54MH074425, U54MH084690, the University of New Mexico Cancer Research and Treatment Center NIH P30 CA118100, the New Mexico Cowboys for Cancer Research Foundation, Oxnard Foundation and the Stranahan Foundation.

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